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USE OF MICROBIAL RISK ASSESSMENT IN SETTING U.S. DRINKING WATER STANDARDS

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This paper outlines US EPA's general strategy for using microbial risk assessment to support the development of US National Primary Drinking Water Regulations (NPDWRs). It discusses specifically the use of such risk assessment in the development of upcoming regulations for disinfection of groundwater (Groundwater Disinfection (GWD) Rule) and for control of disinfectants and their chemical byproducts (Disinfectant/ Disinfection Byproduct (D/DBP) Rule), and possible amendments to the current Surface Water Treatment Rule (SWTR). The risk assessment and risk management processes explicitly consider acceptable risk values for water-borne microbial pathogens. These values directly influence the regulatory choice of treatment levels and methods.

The intention of the US Federal Safe Drinking Water Act is to protect the public from unacceptable health risks arising from drinking water. The Act directs EPA to establish drinking water Maximum Contaminant Level Goals (MCLGs) "at the level at which no known or anticipated adverse effects on the health of persons occur and which allow an adequate margin of safety". EPA policy requires the use of risk assessment in the development of its regulations. MCLGs are not legally enforceable, but point EPA towards health protective regulations. The corresponding NPDWRs are enforceable and are required to be set as close to the MCLG as is technically and economically feasible. They consist of either 1) a Maximum Contaminant Level (MCL) or 2) a treatment technique, if it is not economically or technologically feasible to measure the level of a contaminant in water. The NPDWRs are a product of risk management and include not only risk assessment information, but considerations of analytical capability, monitoring, available treatment technology and costs. They must be health protective.

EPA Regulatory Development

US public health interests require that drinking water be microbiologically safe. This has been taken by EPA to mean not only the prevention of outbreaks of illness, but the minimization of endemic levels of illness. EPA is in the process of developing GWD and D/DBP Rules and re-evaluating the SWTR. The GWD Rule is concerned with

potential health hazards from pathogenic viruses and bacteria in groundwater not under the direct influence of surface water. The goal of the GWD Rule is to protect the public from numerous types of water-borne viruses (e.g., hepatitis A agent, rotavirus, Norwalk and Norwalk-like agents, coxsackieviruses, echovirus) and bacterial pathogens (e.g., Salmonella, Shigella, Campylobacter). The SWTR includes (besides surface water sources) coverage for groundwater sources under the direct influence of surface water. EPA distinguishes this category of groundwater as that which is vulnerable to contamination from protozoa. The goal of the SWTR is to protect the public from pathogenic viruses, bacteria and Giardia lamblia.

The goals of the D/DBP Rule are to ensure that drinking water remains microbiologically safe at the limits set for disinfectants and their byproducts and that the disinfectants and byproducts do not pose an unacceptable risk at these limits. EPA's approach in developing this rule considers the constraints of simultaneously treating for these different pathogen concerns. Considering conventional water treatment methods, any increased chemical disinfection to yield lower microbial risk requires the use of more or stronger disinfectants and, depending upon the point of application and types of byproduct precursors present, may produce higher levels of byproducts, which themselves pose potential health risks. Therefore, risk comparison and risk trade-offs must be considered. EPA has undertaken computer modeling to estimate the relationship of microbial and chemical risks from water treatment. This model examines the magnitude of these risks for a variety of source water qualities and water treatment scenarios.

Two constraints have been imposed as starting conditions for the control of disinfectant and byproduct risks and are considered independently in this analysis: 1) minimally meeting the SWTR as written for disinfection and maintenance of a disinfectant residual in the distribution system, and 2) meeting a potential amended SWTR, termed here an "enhanced SWTR" (ESWTR), which would require higher levels of treatment for Giardia to specifically ensure that the microbial risk at the first customer is less than one infection per 10,000 people per year and that a disinfectant residual is maintained in the distribution system (Gelderloos, et al, 1992). The SWTR currently only requires at least a 99.9 % and 99.99% removal and inactivation of Giardia cysts and viruses respectively prior to the first customer, regardless of sourcewater quality. The ESWTR would follow the EPA SWTR Guidance, which recommends proportionally higher levels of treatment for poorer source waters to achieve the same risk at the first customer for all systems. Within these constraints of disinfection, EPA considers alternatives that achieve acceptable risks from disinfectants and byproducts.

A variety of issues for microbial risk assessment are common to these rules and will be discussed in this paper. These include approaches to microbial risk assessment, development of occurrence data, consideration of comparing microbial risks with those from chemical contaminants, and what acceptable microbial risk levels might be.

Microbial pathogen risk assessment

A number of assumptions have been used in microbial and chemical risk assessments

that are not scientific in origin and are essentially risk management decisions. These are included in the establishment of the appropriate regulatory illness endpoints of concern and the selection of pathogenic organisms for regulation. Additionally, standard, conservative "worst-case" dose-response and exposure assessments are not appropriate to describe this situation where treatment to decrease exposure to microbial pathogens in drinking water may increase exposure to chemical contaminants.

Illness endpoints of concern

The possible microbial illnesses, or "endpoints of concern", vary with the organism and vary markedly in their severity. In EPA's previous drinking water regulations involving pathogenic organisms (i.e., Total Coliform Rule and SWTR), these endpoints have been taken together as a broadly generalized "microbial illness" resulting from these organisms in total, rather than as separate defined illnesses attributable to specific organisms. The intention of these regulations was to minimize all microbial illnesses. The most common microbial illness, gastrointestinal illness or diarrhea, is generally considered non-life threatening in normally healthy adults. However, the US Centers for Disease Control (CDC) have presented data that indicate overall death rates from gastrointestinal illness from a variety of organisms approach 0.1% (Bennett, et al, 1987). In addition, studies (Glass, et al, 1991; Lew, et al, 1991) indicate that sensitive subpopulations, including infants and those over 70 years old, have mortalities of 3-5% from diarrhea requiring hospitalization. Additionally, specific pathogenic organisms produce illness endpoints more serious than gastrointestinal illness. Hepatitis A infections, for example, may lead to jaundice and liver damage, as well as death. Death rates from hepatitis A illnesses in the U.S. have been reported at 0.6% of those who are ill (CDC, 1985). Incidence and mortality information for a variety of waterborne disease agents are found in Tables A and B. As a result of this, EPA is considering risk assessments for a variety of organisms and illness endpoints.

Infection vs. illness

Microbial dose-response determinations try to relate ingested levels of organisms to a given detection endpoint. This may be demonstrable infection or symptomatic illness or some other measure. In the interest of protecting public health in a diverse population, EPA has focused on preventing infections and has considered defining acceptable risk with respect to infections avoided. For example, the goal of EPA's Surface Water Treatment Rule was to achieve risk reduction with respect to microbial infection (USEPA, 1989). Generally, however, infection is not equal to illness. As an example, in the Rendtorff (1954) study on the infectious dose for Giardia, many healthy individuals became infected, as shown by cysts in stool samples, but none became ill. A survey of a waterborne outbreak of giardiasis in Berlin, NH, showed 76% of the infections were asymptomatic. Only 3% of those infected required hospitalization (Lopez, et al, 1980). For Vibrio cholerae 01 (the toxigenic Latin American strain), 75% of infections are asymptomatic. Some 20% of those infected develop mild diarrhea and only 5% develop the severe, clinically-recognized form of the disease (CDC, 1991). It is understood, however, that sensitivity to microbial illness includes enhanced likelihood of significant illness after infection. To be protective of the overall public health, EPA focuses on adverse effects to the sensitive subpopulations (in this

case, infants and the elderly), thus EPA believes that by controling microbial pathogens with respect to some acceptable level of infection rather than illness provides greater protection to all.

EPA also assumes that the susceptibility to infection of the population studied by researchers (i.e., male prisoners, students) is representative of the U.S. population as a whole. However, whether an individual becomes infected depends upon pathogen virulence and dose, as well as the health of the individual. While an infectious unit may represent a single virus particle (Katz and Plotkin, 1967) or Giardia cyst, frequently much higher doses, especially for bacterial pathogens, are required to yield an infection. These variations are difficult, if not impossible to determine. For risk assessment purposes, EPA assumes for Giardia and viruses that a dose of one infectious unit can yield an infection. Using the dose-response curve developed from the Rendtorff data (Rose, et al, 1991), this translates to about a 2% chance for an individual to become infected if one Giardia cyst is ingested.

Selection of appropriate pathogenic organisms for regulatory development

In the development of the SWTR, EPA selected Giardia as the representative organism for risk assessment, regulation and treatment. Giardia was selected because data was available for risk assessment and because it was perceived that Giardia was more resistant to disinfection than most other known microbial pathogens in water. It was assumed that adequate disinfection of Giardia would yield adequate disinfection for most other microorganisms of concern. Recent data suggest that Cryptosporidium, because of its greater resistence to disinfection than Giardia, may be a more appropriate target organism for defining adequate levels of treatment.

Protozoan pathogens, such as Cryptosporidium or Giardia, are not normally found in true groundwaters not under the direct influence of surface water. The pathogens of concern in groundwaters only include enteric viruses and bacteria. EPA considers viruses as more difficult to disinfect than bacteria, thus has selected representative viruses for risk assessment and regulatory purposes. At issue are both general and specific problems in defining risk from waterborne viral infection. EPA had considered using a single virus or virus group as the basis for determining risk, but rejected this approach because no one virus appeared suitable. Complicating the selection of a single virus for calculating risk is the fact that occurrence data for pathogenic viruses in water are scant, primarily from outbreak investigations. Moreover, dose-response data are only available for a few viruses and the relative occurrence in water for different viruses may vary over time, depending on the prevalence of a particular viral disease in nearby populations that influence the source water quality. Additionally, sensitivities to different disinfectants vary between viruses. Rotaviruses, for example, are more sensitive to chlorine than hepatitis A, but less sensitive than hepatitis A to chloramine.

Hepatitis A represents the greatest health threat in terms of severity of waterborne illness (short of death) and is more resistant to disinfection than many other pathogens. Unfortunately, no practical enumeration method for hepatitis A in drinking water and no dose-response data are yet available. This prevents a quantitative risk assessment based on this organism. In contrast, rotaviruses have a lower infectious dose than most other waterborne viruses, and dose-response data are available, but

the disease is not as severe as that from hepatitis A.

As a result of these complications, EPA is considering use of a conceptual "synthetic virus" of combined properties for regulatory development, as described by Regli, et al (1991), which would provide reasonable worst-case limits for any given virus. This concept would combine the properties of several pathogenic waterborne viruses to define a reasonable worse-case situation. EPA would use the enterovirus group (poliovirus, echovirus, coxsackievirus) to determine waterborne occurrence, since relatively simple quantitation methods exist and this measurement would represent worst case occurrence for any particular enteric virus; rotaviruses for calculating dose-response; and hepatitis A to estimate disinfection efficiency.

Determination of organism concentration in finished water

Risk estimates from exposure must ultimately be based on pathogen concentrations in water reaching consumers. It is not possible to practically measure pathogen concentrations (at least for Giardia and viruses, since they are health concerns at very low concentrations) in finished water to demonstrate that acceptable risk levels are being achieved (Regli, et al, 1991). It is much more practical to monitor the source water for pathogens or to estimate such concentrations indirectly (e.g., by measuring virus concentrations in septic tanks or sewer lines and estimating die-off and dilution in the source water), determine the level of treatment provided and then estimate the organism occurrence in finished water. These estimates can be used to calculate the associated risk and determine whether the treatment in place is adequate. This indirect approach, however, introduces the uncertainty of estimating treatment efficiencies in addition to characterizing the occurrence in the source water. This approach also cannot be used to quantify risk from bacterial pathogens which may regrow in the distribution system. The assumption that these uncertainties are acceptable, or can be reasonably defined, is a major caveat to EPA's current risk assessment approach. Depending on specific conditions, the uncertainties in the quantified risks may span several orders of magnitude.

Comparing pathogenic microbial risk and chemical risk

As part of rule development, EPA is comparing human health risks of microbial illness with risks from disinfectants used to minimize these microbial risks and risks from the resulting disinfectant byproducts. This comparison is difficult in that risks from pathogenic microorganisms are generally acute versus those from chemicals, which are generally chronic. Also, risks from microorganisms are not calculated in the same manner as are those from chemical contaminants, thus they are not explicitly comparable. However, similarities do exist and with some care, approximate comparisons can be made.

One difficulty is that agents and their adverse effects are considered differently for microoganisms and chemicals. The possible microbial illnesses, or "endpoints of concern", vary with the organism and vary markedly in their severity. As discussed above, these endpoints have been taken together as a broadly generalized "microbial illness" resulting from these organisms in total, rather than as separately defined

illnesses attributable to specific organisms. This is different from EPA's treatment of chemical contaminants, where individual chemicals or closely related chemicals are regulated separately. Also, each chemical is regulated to one specific endpoint of concern. For chemicals judged to be known or probable human carcinogens, the endpoint of concern is cancer, leading to premature mortality. For non-carcinogenic chemicals, a specific adverse endpoint of concern is identified in the Reference Dose determination. This endpoint is generally at the lower end of a severity progression.

Derivation of dose-response data also differs between microorganisms and chemicals. For microbial pathogens, dose-response values are determined directly from data on human infection or illness. Microbial illnesses are usually rapid and acute, and thus can be causally linked to the infecting organism. Epidemiological data from disease outbreaks attributed to pathogenic organisms in drinking water can in some cases be correlated to the organisms' ambient levels. The studies by Rendtorff (1954), which have been used to derive dose-response values for Giardia infection, involved human subjects given known amounts of Giardia cysts. The viral dose-response relationships described by Regli, et al (1991) were likewise derived from studies of human populations (Lepow, et al, 1962; Katz and Plotkin, 1967; Minor, et al 1981; Schiff, et al, 1984; Ward, et al, 1986).

Chemical dose-response assessments are far less certain. For chemical contaminants, such as the disinfectants and disinfection byproducts, which occur at less than part per million or billion levels in drinking water, resulting illnesses of concern are chronic and are expected to appear only after long exposures. Causal linkage of illness to these low exposures is impossible. Further, current EPA methods to determine chemical dose-response values generally extrapolate data from high exposures in laboratory animals to the low exposures expected for humans. These extrapolations use health-conservative methods that may add orders-of-magnitude safety factors and result in considerable uncertainty. For known animal carcinogens, it is currently assumed that no exposure threshold exists and any exposure poses a risk. The resulting theoretical 95% upper-bound lifetime human cancer risk is estimated such that the real risk is unlikely to be greater than the calculated value, is almost certainly lower, and may be zero. However, since in at least some instances one infectious unit can yield illness, microbial risk from protozoa and viruses could also be considered to be without a threshold, thus allowing probability estimations in the same manner as with chemical carcinogens. Comparison of microbial risks with those from non-carcinogenic chemical contaminants poses other problems. Endpoints of concern are not the same and may differ substantially in their severity and the progression of severity with increasing doses. Probability-based dose-response values for these contaminants cannot be calculated using current risk methods standard at EPA.

Exposure data are generally stronger for chemical contaminants than for microbial pathogens. Chemicals can be assayed routinely to part per billion or greater sensitivity and plausible chronic exposures can be estimated from this data. However, it is much more difficult to estimate exposures to pathogenic microorganisms to allow calculation of endemic risk. Many pathogenic microorganisms lack reliable and sensitive quantitation methods for occurrence levels typically seen in water and levels of occurrence can vary several orders of magnitude at a given site. We desire occurrence data to allow estimation of endemic levels of microbial illnesses. While

epidemiological data exist for microbial illness, reported data are from outbreaks in communities and do not indicate endemic levels of disease. Additionally, most workers in the field believe that substantial underreporting of illness outbreak occurs.

Modeling of pathogen, disinfectant and disinfection byproduct risks

EPA has undertaken mathematical modeling intended, in part, to produce estimates of pathogen and chemical exposures and risks to individuals arising from a variety of source waters after various water treatments. EPA desires that these estimates approximate the distributions that occur nationally. These models simulate occurrence levels of pathogenic organisms (specifically Giardia) in raw water, then simulate removal efficiencies of pathogens and production of disinfection byproducts. The microbial and chemical concentrations thus generated are then used to estimate potential health risks. By considering a variety of increasingly stringent regulatory options and treatment trains, relative changes in microbial and chemical risks can be estimated and considered. There are a number of assumptions and uncertainties in these models. Input occurrence data is discussed below. Issues for dose-response determinations have been discussed above.

Waterborne pathogens in surface waters include protozoa (e.g., Giardia, Cryptosporidium), bacteria (e.g., Legionella, Salmonella, Campylobacter), enteric viruses (e.g., Norwalk and Norwalk-like agents, rotaviruses, hepatitis A agent), and blue-green algae. In the SWTR, EPA specified treatment to eliminate Giardia cysts, and assumed that treatment values were sufficiently high to control other microbial contaminants in surface water. In contrast, the pathogens generally occurring in groundwater only include enteric viruses and bacteria. For groundwater, EPA's concern is for viruses, since Giardia and Cryptosporidium are not present and viruses are generally more resistant to disinfection than the pathogenic bacteria. However, source water occurrence data for all pathogenic microorganisms but Giardia and Cryptosporidium are scant. Therefore, EPA has focused on surface waters and Giardia in the development of the comparative risk assessment.

The overall purpose of this modeling effort is to determine the likely exposures to pathogens and chemical contaminants remaining after water treatment, for typical water treatment process trains, raw water quality characteristics and modeled raw water pathogen levels. EPA considered five treatments for surface water and five for groundwater as describing the majority of public water supply systems. Depending on the treatment scenario, various reductions of Giardia and virus levels occur during treatment. Assumptions for the water treatment trains are derived from the SWTR. CT values for Giardia and hepatitus A were used. One hundred simulations of annual city means for Giardia and disinfection byproducts (trihalomethanes and haloacetic acids) in finished water were generated and used in subsequent risk assessment. Since EPA currently lacks appropriate virus occurrence data, only the modeling for Giardia in surface water systems has been performed.

Preliminary work reported by Grubbs, et al (1992) examined the two levels of surface water treatment described above, one minimally meeting the SWTR and the other meeting an ESWTR, where higher levels of treatment are specified for poorer quality source waters. The results indicated that systems only minimally meeting SWTR

standards of 3-log disinfection of Giardia could still produce water yielding significant endemic levels of microbial illness, depending upon the Giardia cyst concentrations that occur in source waters. Increasing treatment proportionally for systems with higher Giardia cyst concentrations to achieve approximately the same average Giardia concentration at the first customer, reduced modeled endemic illness to de minimus levels without substantial increases in treatment costs and without an appreciable increase in disinfection byproduct levels. This could reasonably be expected to apply to disinfection of bacteria and viruses as well, owing to their higher sensitivity to disinfection. Comparison of appropriate model results to CDC data and to waterborne outbreak disease data (Grubbs, et al, 1992) appears to support the validity of the model and suggests that this model may be valuable for these analyses.

Acceptable human health risk

EPA is concerned with acceptable levels of public health risk from drinking water pathogens. The current approach in developing these rules considers a requirement for an acceptable microbial risk, reflected in a promulgated MCL or treatment technique, that can feasibly be obtained. This differs from a MCLG, which is an aspirational goal that does not take feasibility into account. MCLGs for pathogenic organisms are generally set at zero, indicating that no risk of illness is the desired goal. This is similar to the approach taken for regulating chemical carcinogens, where MCLs are set as close to the MCLG of zero as is technically and economically feasible, but also within an acceptable cancer risk range from 10^{-4} to 10^{-6}. Whether an acceptable risk is achieved can be determined from risk calculations. For these purposes, the prevention of endemic illness is a concern, in addition to prevention of illness outbreaks in a community.

For the SWTR, a risk of one infection per 10,000 people per year was taken as the acceptable health goal for Giardia. CDC data (Bennett, et al, 1987) indicate that Giardia contributes about 8% (70,000 of 940,000) of all water-borne microbial illness. Given a 70 year lifespan, this calculates to a mean average 10% lifetime risk for microbial infection from drinking water. Based on estimations from the maximum likelihood analysis of Giardia occurrence reported by Grubbs, et al (1992), the 95% upper-bound risk would be on the order of 10-fold higher, thus yielding an estimated lifetime risk of infection of 1. At this level of total infection, the lifetime risk of death from waterborne microbial illness can be estimated. Using the CDC (Bennett, al al, 1987) ratio of approximately 0.1% for mortality resulting from waterborne microbial illnesses and assuming that all infections cause illness, then the estimated upper-bound lifetime risk for this would be10^{-3}. If the mean risk value for infection was used along with a plausible illness to infection ratio of 10^{-1}, mean lifetime risk of death would be about 10^{-5}.

Noting that significant differences exist in how risks are calculated and interpreted for microorganisms, relative to chemical contaminants, the above developed acceptable microbial risks can be roughly compared to the acceptable levels for chemical contaminants, as represented by EPA drinking water MCLs. For carcinogens, MCLs are general set from about 1×10^{-4} to 1×10^{-6} theoretical 95% upper-bound lifetime cancer risk.

Implications for US drinking water policy

An immediate implication of this work is the realization that microbial pathogens continue to dominate the comparative water-borne human health risks. Underscoring this is recent work of Payment, et al (1991), which found that a water system meeting existing microbial drinking water standards could have endemic water-borne illness rates of 25-35% per year. This focuses more regulatory attention towards enhancing disinfection via a GWD Rule and a possibly stricter SWTR, rather than accepting current standards as adequate. It also directs research towards outstanding problems in microbial analysis, risk assessment and treatment technologies.

Treatment technology is of particular importance in terms of regulatory feasibility. If the risk estimations and comparisons are valid and predictive, it should be possible to determine a minimum point for the sum of microbial and disinfection risks for a given level of treatment. To the limit of feasibility, this minimum could be lowered by requiring higher levels of treatment to not only disinfect, but to reduce disinfectant dosages and residuals and resultant byproducts. Feasibility in this case may be limited by technology as well as by economics. For example, current treatment using conventional filtration processes and adequate chemical disinfection contact time to minimize microbial risks, followed by carbon filtration to remove byproducts, may still yield substantial disinfection byproduct risks in some systems with poor source water quality. Use of membrane filtration to physically remove microbial pathogens (including viruses) produces no known byproducts of concern, and would be of minimum risk even when followed by a residual disinfectant in the distribution system. However, membrane filtration technology is not yet feasible for all systems and involves high costs as well as potential water wastage. Policy implications here are toward maintaining adequate disinfection relative to control of disinfectants and disinfection byproducts to the limits of technology at a given time. As technology progresses, driven by a goal of overall drinking water risk minimization, more stringent controls on disinfection byproducts may be possible without sacrificing disinfection. Ultrafiltration, because it removes virtually all microbial pathogens, followed by chloramine as a distribution system disinfectant, may be a long-term solution, especially for bromide-containing source waters, if health risks from chloramine byproducts do not prove to be significant.

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Table A Water-borne Domestic Microbial Infections, 1985

Disease or agent	Incidence	Fatality/case (%)
Total Water-borne	940,000	0.1
Campylobacteriosis	320,000	0.1
E. coli	150,000	0.2
Misc. enteric	10,000	1.0
Salmonella, nontyphi.	60,000	0.1
Shigella	30,000	0.2
Typhoid	60	6.0
Vibrio (excl. Cholera)	1,000	4.0
Yersiniosis (excl. plague)	1,800	0.05
Norwalk	300,000	0.0001
Giardia	70,000	0.0001

Data calculated from Bennett, et al (1987)

Table B Suspected Water-borne Diseases and Organisms

Disease or agent	Fatality/ case (%)
Cholera	1.0
Legioneliosis	15
Enteroviral disease (excl. polio)	0.001
Hepatitis A	0.3
Poliomyelitis	10
Rotavirus	0.01
Coxsackieviruses	-
Echovirus	-
Reovirus	-

Data from Bennett, et al (1987)